UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ENZO BIOCHEM, INC. and ENZO LIFE SCIENCES, INC., Plaintiffs, - against - MOLECULAR PROBES, INC., Defendant. - and - YALE UNIVERSITY, Nominal Defendant.	)	03 CV 3816 (RJS)

PLAINTIFF ENZO'S RESPONSE TO MPI'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NON-INFRINGEMENT AND CROSS-MOTION ON CLAIM CONSTRUCTION AND PARTIAL SUMMARY JUDGMENT OF VALIDITY

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Plaintiffs Enzo Biochem, Inc. and Enzo Life Sciences, Inc. (collectively, "Enzo") respectfully submit this response to Defendant Molecular Probes, Inc.'s ("MPI's") motion for partial summary judgment on Enzo's infringement claims against MPI's ULYSIS products ("the Motion"). Enzo disputes and opposes MPI's legally erroneous claim construction because it misstates Enzo's construction, seeking a "disclaimer" based on only snippets of statements made by Enzo in the still-pending PTO reexamination (and the Court years ago), and hereby cross-moves for partial summary judgment of validity of U.S. Patent No. 5,241,060 ("the '060 patent") under a proper claim construction which accounts for, and is supported by: the intrinsic evidence of the '060 patent, the clear purpose of the invention, and the full context of the actual statements that have been made by Enzo in the reexamination and throughout this lawsuit.

PRELIMINARY STATEMENT

Enzo has accused certain MPI products, specifically MPI's ChromaTide and Ulysis products, of infringing upon Enzo's '060 patent. MPI now moves for partial summary judgment that its Ulysis products do not infringe. In doing so, MPI miscasts the claim construction that has been advanced by Enzo, but not yet adopted by the Court, with regard to Enzo's '060 patent. MPI presumably does this to gain advantage, or at least to preserve arguments that the '060 claims are invalid over the prior art in order to protect its still-accused ChromaTide products.

Enzo concedes that—should the construction that it has actually been arguing from the very beginning of this suit be adopted by this Court—the Ulysis products do not infringe. At the same time, however, that construction would also dispose of MPI's prior art invalidity defenses raised in this suit and in the Reexamination. That is why, in an effort to obviate this Motion before it was filed, and to further streamline the case for trial, Enzo offered a stipulation ("the

Stipulation") to MPI proposing: (i) the construction of the claims-at-issue[1] which Enzo has actually and consistently put forward throughout this suit; and (ii) dismissal of its infringement claim against ULYSIS under that construction.[2] MPI rejected Enzo's proposed construction, filed its Motion, and argued that there is no dispute over claim construction—without mention of the Stipulation and/or the prior summary judgment proceedings before Judge Sprizzo where MPI also undeniably disputed Enzo's construction—all in an effort to convince the Court that summary judgment can be decided without any need to construe the claims beforehand.

But, because the construction of the Claims is and has always been disputed, the law is clear that this Court must first rule on the proper construction of Enzo's '060 patent claims for purposes of both infringement and validity before reaching any determination on those issues. MPI cannot have it both ways—i.e., bind Enzo to an incomplete claim construction based on cherry-picked snippets of statements from Enzo's reexamination response ("the Response") in order to remove its ULYSIS products from the case, while leaving itself room to argue a broader construction than Enzo's actual statements (more than 26 times!) to the PTO in order to keep alive MPI's inconsistent prior art invalidity defenses. Accordingly, Enzo respectfully submits the following memorandum in response to MPI's Motion and in support of Enzo's cross-motion for construction of the Claims and partial summary judgment on MPI's prior art invalidity defense.

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[1] Contrary to MPI's suggestion (*see* Memorandum of Law in Support of MPI's Motion ("the Brief") at 1), Enzo accused the ULYSIS products of infringing claims 1-3 of the '060 patent ("the Claims"). (Ex. 1, 5/17/05 Enzo Infringement Contentions; Decl. of Eric M. Jaegers in Support of MPI's Motion ("Jaegers Decl."), Ex. 4 at 42; *see also* Ex. 2, '060 patent, col. 31, lines 14-32.) Unless otherwise indicated, all exhibits cited herein are exhibits to the Declaration of Jennifer R. Moore submitted in support of Enzo's Response to MPI's Motion and Cross-Motion.

[2] What Enzo actually told the PTO multiple times, and proposed in its pre-Motion Stipulation to MPI, is that the Claims require attachment of a label to a mononucleotide that is capable of being incorporated into a nucleic acid that is ***for use as a hybridation probe***.

PROCEDURAL AND FACTUAL BACKGROUND

I. MPI's Past Summary Judgment Tactics And Enzo's Claim Construction

In early 2007, MPI moved for summary judgment of invalidity, alleging that the same three (3) prior art references presently at issue in the '060 patent reexamination — the Draper, Eshaghpour and Faust articles — "anticipate" the '060 patent ("the Invalidity MSJ"). (Ex. 3, 1/3/07 Defendants' Memo of Law in Support of Invalidity MSJ at 33; Ex. 4, Draper (1980); Ex. 5, Eshaghpour (1979); Ex. 6, Faust (1974).) In opposition, Enzo argued that the references did not anticipate, *inter alia*, because:

> Nevertheless the Court correctly noted that the '060 patent describes "special nucleotides." (*Id*.) The specification of the '060 patent makes clear from the outset that the special ***nucleotides required by claim 1 must be useful for making probes*** and must be labeled in a non-disruptive manner …. *Specifically, the nucleotides disclosed in these references are unable to be incorporated into a polynucleotide and* ***are not useful as a probe***.

(Ex.7, 5/15/07 Enzo Mem. in Opp. to Invalidity MSJ at p. 35) (emphasis added). MPI undeniably disputed Enzo's above-proposed construction of the Claims in its 2007 Reply brief, arguing that:

> However, as an initial matter, ***Enzo's arguments are based entirely on an improper reading of functional limitations into '060 claim 1 – i.e., that the claim 1 nucleotide is required to be*** "incorporated into a polynucleotide" and to be ***"useful as a probe."*** See Opp. at 35…. Enzo is ***wrong*** on both counts.

(Ex. 8, 6/15/07 Defendants' Reply Memo on Invalidity MSJ at p. 21) (emphasis added). MPI also never raised a non-infringement issue with respect to this disputed claim construction. Then, after Judge Sprizzo indicated that he was unlikely to grant MPI's Invalidity MSJ, MPI formally withdrew it. (Ex. 9, 7/17/07 H'rg Tr. 87:4-88:10.) Subsequently, this Court denied both of MPI's attempts in 2011 and 2012 to resurrect its withdrawn Invalidity MSJ (Ex. 10, 8/22/11 Hr'g Tr. 18:21-19:14; and Ex. 11, 11/16/12 Hr'g Tr. 44:25-45:3,49:4-24) – and MPI once again made the tactical decision not to seek summary judgment of non-infringement based on Enzo's proposed construction despite having been given a second chance by this Court to do so (Ex. 10 at 23:13-

16). Instead, MPI repackaged its Invalidity MSJ into a PTO reexamination request on June 15, 2013, citing the same prior art, and submitting the same expert declaration previously filed/withdrawn in this lawsuit. (Jaegers Decl. Ex. 7 at 1-4.)

II. The Still-Pending Reexamination Proceedings And Enzo's Actual Statements To The PTO About The Scope Of The '060 Patent Claims Being Limited To "Hybridization Probes" And The Failure Of MPI's Prior Art To Disclose It

In Response to the prior art invalidity arguments raised by MPI, Enzo repeatedly stated to the PTO that the Claims of the '060 patent require the labeled mononucleotides of the Claims to be capable of incorporation into an oligo- or polynucleotide for use as a hybridization probe[3] and, as a consequence, none of MPI's allegedly invalidating references—Draper, Eshaghpour, and Faust (Exs. 4-6)—anticipates those Claims. (Ex. 12, Response at 9-14, 16-17; Ex. 13, Rokita Decl. ¶¶ 8, 10-17, 22-24.) The fact of the matter is, Enzo's submission to the PTO makes reference to this hybridization probe limitation of the Claims more than 40 times (26 mentions in Enzo's Response, Ex.12; and 16 in the supporting Rokita Declaration, Ex. 13) in distinguishing MPI's prior art. MPI's Motion carefully omits this hybridization probe aspect of Enzo's claim construction and arguments with respect to MPI's prior art. Those arguments are detailed below for purposes of this response to the Motion as well as Enzo's cross-motion for summary judgment, with MPI's tactical carve-outs of the relevant parts of Enzo's Response highlighted. (*See* pp. 7-13, *infra*.)

[3] Hybridization of nucleic acids (i.e., oligo- or polynucleotides such as DNA, RNA, etc) is a process that involves the formation of a double-stranded DNA, RNA, or RNA-DNA hybrid from two individual complementary oligo- or polynucleotides. (Ex. 14, 5/15/07 Sinden Decl. ¶ 26.) To detect a target nucleic acid, one adds a hybridization probe (a short piece of DNA or RNA labeled as described in the '060 patent) to a sample of nucleic acids and then the probe hybridizes with a target DNA sequence. (*Id.* ¶¶ 27-28.)

III. Enzo's Proposed Stipulation To MPI Should Have Obviated This Motion

In an effort to avoid burdening the Court and parties with further summary judgment briefing and proceedings, Enzo reached out to MPI on July 8, 2013, concerning MPI's contemplated motion for summary judgment of non-infringement, the accused ULYSIS products, and the actual prior art-distinguishing statements in Enzo's reexamination Response. (MPI Brief at 1; Ex. 15 (July 2013 emails between the parties) at 3.) Enzo proposed that—to the extent MPI were willing to agree upon the scope of the claims that was actually argued by Enzo during the pending PTO reexamination—Enzo would agree to a dismissal of its infringement claims against MPI's ULYSIS products. During the parties' meet and confer discussions, however, MPI told Enzo that it did not believe MPI needed to take a position on claim scope in order to prevail on its contemplated Motion (which probably explains why the Motion's proposed Order does not contain one). MPI further requested that Enzo reduce the Stipulation to writing, which Enzo did the next day, proposing the following scope of the Claims:

> The labeled mononucleotides of the Claims of the '060 patent must exist independently prior to their incorporation into an oligo- or polynucleotide hybridization probe.

(Ex. 16 (7/17/13 Proposed Stipulation).) MPI waited until the day the Motion was due to reject the Stipulation without explanation. (Ex. 15 at 1.) If anything, MPI's rejection of Enzo's proposed construction, by itself dispels any notion that there is no dispute over claim construction. MPI's suggestion to the contrary in its Motion in an attempt to circumvent the legally-mandated claim construction process. (Brief at 6; *see also*, again, the claim construction dispute in MPI's Invalidity MSJ Reply brief, *supra* at p. 3.)

ARGUMENT

I. The Relevant Legal Claim Construction Standards For Purposes Of Both Infringement and Validity

The law is clear. Determinations of both infringement and invalidity require the same two step analysis. *Amgen Inc. v. Hoechst Marion Roussel, Inc.,* 314 F.3d 1313, 1330 (Fed. Cir. 2003) ("It is axiomatic that claims are construed the same way for both invalidity and infringement.") Indeed, because the claims of a patent define the scope of the invention at issue, the claims must **first** be interpreted and given the **same** meaning by the Court as a matter of law for purposes of **both** validity and infringement analyses. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001) (abrogated on other grounds). Next, the properly construed claim is compared with either: (i) the accused product(s) (for infringement), or (ii) the prior art reference(s) (for invalidity), to determine whether all of the claim limitations are met or disclosed for purposes of infringement or invalidity, respectively. *Id*. A patent is presumed valid by statute. *Union Carbide Chem. & Plastics Tech. Corp. v. Shell Oil Co.*, 308 F.3d 1167, 1185 (Fed. Cir. 2002). Thus, for purposes of "anticipation" by the prior art, as MPI argues in this lawsuit and the PTO Reexamination, the defendant must prove by clear and convincing evidence that each and every element of the patent claims is disclosed in a single reference. *Id*. at 1188; *Leighton Tech. LLC v. Oberthur Card Sys.*, S.A., 423 F. Supp. 2d 425, 430 (S.D.N.Y. 2006) (citation omitted) (anticipation "requires that the four corners of a single, prior art document describe every element of the claimed invention.") The absence of even a single element from the prior art defeats an anticipation defense. *Union Carbide*, 308 F.3d at 1189. This two-step analysis must be conducted, including on summary judgment, and cannot be bypassed. *Grober v. Mako Products, Inc.*, 686 F.3d 1335, 1344 (Fed. Cir. 2012).

Moreover, when "the parties present a fundamental dispute regarding the ***scope*** of a claim term, it is the court's duty to resolve it" as a threshold matter. *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1361-62 (Fed. Cir. 2008). As part of that claim construction analysis, the Court must consider the intrinsic evidence of the language of the patent claims and specification in the first instance, as well as what MPI refers to as "binding and inescapable intrinsic evidence" (D.I. 116 (6/25/13 MPI Letter) at 5) of the proceedings before the PTO. *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). Where a Court finds as a matter of law that a prosecution disclaimer limits claim scope, such disclaimer narrows the ordinary meaning of the claim "congruent with the scope of the surrender." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1321; *see also Chimie v. PPG Indus. Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005) (citing *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576, 1580 (Fed. Cir. 1988) ("The purpose of consulting the prosecution history in construing a claim is to 'exclude any interpretation that was disclaimed during prosecution.'") The scope of any disclaimer must be based on the nature and overall context of all of the statements made by the patentee. *Cordis Corp. v. Medtronic Ave, Inc.*, 511 F.3d 1157, 1177 (Fed. Cir. 2008); *Seachange Int'l, Inc. v. C-Cor, Inc.*, 413 F.3d 1361, 1372 (Fed. Cir. 2005) (must examine "all arguments to overcome and distinguish references"); *Read Corp. v. Portec, Inc.*, 970 F.2d 816, 824 (Fed. Cir. 1992).

II. MPI's Reliance on Isolated Snippets of Statements to the PTO as Claim Scope Disclaimers Must Be Rejected

MPI's Motion should be rejected for multiple reasons. First, MPI seeks to obtain summary judgment without having the Court construe the scope of the Claims (and any alleged disclaimer thereof) based on an untenable premise that there is no dispute over claim construction. (MPI Brief at 6.) This is not, and clearly has not ever been the case—as evidenced

by MPI's rejection of Enzo's proposed Stipulation and/or the contested Invalidity MSJ that MPI dropped back in 2007. (*See* pp. 3 and 5, *supra*.)

Second, MPI also asks this Court to commit legal error by imposing a prosecution history disclaimer that is not consistent with the statements ***actually made*** by Enzo in the Response. Indeed, MPI's Brief advocates a claim construction based on repeated incomplete characterizations of Enzo's statements, quoting only portions of the Response (MPI Brief at 3 quoting Response at 6-7) while omitting other statements, and even parts of sentences containing the relevant "hybridization" and "probe" language. As can be seen from the below example - which is only one of several in MPI's brief - Defendant's quote to the Court cuts out the relevant shaded parts of a sentence regarding the hybridization probe aspect of Enzo's statements:

> More particularly, the patent relates to **hybridization probes** that are formed by *first* label[] a mononucleotide with a detectable moiety …, and *subsequently* incorporating the labeled mononucleotide into an oligo- or polynucleotide **probe**

(MPI Brief at 10) (shading and bold added to highlight text omitted from quote by MPI, italics and underline in MPI's quote.) Likewise, MPI tactically omitted entire sections (shaded below) of Enzo's Response (containing at least a half dozen references to "hybridization" and "probes") including, as can be seen below, relevant sections immediately preceding MPI's block quote:

> V.The '060 Patent
>
> Generally, **the '060 Patent relates to hybridizations probes**. (See col. 2, lines 57-62: "In accordance with the practices of this invention nucleotides are modified . . . preparatory for the preparation therefrom of nucleotide probes suitable for attachment to or incorporation into DNA or other nucleic acid material" (emphasis added)) and col. 25, lines 11-16: "A particularly important and useful aspect of the special nucleotides of this invention is the **use of such nucleotides in the preparation of DNA or RNA probes. Such probes** would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified."). The application as originally filed specifically stated that the "modified polynucleotides" are **used in "hybridization probes,"** including "gene mapping in situ hybridization" and further provides a "General Protocol For

MPI BLOCK QUOTE STARTS HERE →

> Probe Detection Via In Situ, Colony, or Northern / Southern **Hybridization** Methods." (pp. 27-29). Based on the above, Dr. Rokita explains that one skilled in the art would understand that the oligo- and polynucleotide **probes of the '060 Patent claims must be capable of use as hybridization probes**. (See Rokita Decl. ¶ 8).
>
> More particularly, the patent relates to hybridization probes that are formed by first labeling a mononucleotide with a detectable moiety (termed "Sig" in the patent), and subsequently incorporating the labeled mononucleotide into an oligo- or polynucleotide probe using a polymerase (e.g., a terminal transferase). (See col. 2, lines 57-62; col. 25, lines 41-48)….

(*Id.* at 3 (citing Response at 6-7); shading and bold added to highlight statements omitted from quote.) This improper cherry-picking of only certain parts of Enzo's statements, while tactically omitting other statements that undeniably dispose of MPI's prior art invalidity defenses is contrary to the law which requires Courts to construe the Claims, and any alleged disclaimers, congruent with the entirety of Enzo's statements as to the scope of the Claims. *Omega Eng'g, Inc.*, 334 F.3d at 1321 ("the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender.")

III. Enzo's Construction – As Previously Presented To This Court And In The Still-Pending PTO Reexamination - Is Fully Supported By The Intrinsic Evidence

Unlike MPI's proposed construction, the intrinsic record fully supports the consistent claim construction Enzo has long urged in this case, and now asks the PTO and this Court to adopt and apply: "*The labeled mononucleotides of the Claims of the '060 patent must exist independently prior to their incorporation into an oligo- or polynucleotide hybridization probe*."

Indeed, as explained above, this construction is not only congruent with Enzo's positions and statements presented to the PTO, but is also fully supported by the intrinsic evidence of the patent specification and file history, as detailed in Enzo's Response:

> Generally, ***the '060 Patent relates to hybridizations probes***. (*See* col. 2, lines 57-62: "In accordance with the practices of this invention nucleotides are modified . . . preparatory for the preparation therefrom of nucleotide probes suitable for attachment to or incorporation into DNA or other nucleic acid material" (emphasis added)) and col. 25, lines 11-16: "***A particularly important and useful***

> ***aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes. Such probes*** would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified."). The application as originally filed specifically stated that the "modified polynucleotides" are ***used in "hybridization probes,"*** including "gene mapping in situ hybridization" and further provides a "General Protocol For Probe Detection Via In Situ, Colony, or Northern / Southern Hybridization Methods." (pp. 27-29). Based on the above, Dr. Rokita explains that one skilled in the art would understand that the oligo- and polynucleotide ***probes of the '060 Patent claims must be capable of use as hybridization probes***. (*See* Rokita Decl. ¶ 8).

(Ex. 12 (Response), *e.g.*, at 6, 9 (referring to the hybridization probe requirement 26 times); *see also* Ex. 2, '060 patent, at *e.g.*, col. 2, line 56 to col. 3, line 14; col. 24, lines 17-23; col. 25, lines 11-48; Ex. 17 ('060 original patent application stating the "modified polynucleotides" are used in "hybridization probes" and providing a "General Protocol for Probe Detection Via *In Situ*, Colony, or Northern/Southern Hybridization Methods"); Ex. 18, 5/15/07 MPI's Keana Tr. 72:18-75:7; 88:17-89:19; 92:9-93:17; 114:1-24.) Indeed, in support thereof, Dr. Rokita mentions the "hybridization probe" requirement of the Claims 16 times, and includes an entire section entitled, "Claim Construction" (Ex. 13 ¶¶ 6 and 1-5), in which he gives his expert opinion that a person of skill in the art would construe the Claims in a manner consistent with Enzo's position:

> **I. Claim Construction**
>
> * * * *
>
> 8. It is also my opinion that ***claims 1-3 of the '060 Patent require that the labeled nucleotides be useful for making hybridization probes***. This is supported by the Patent itself which teaches that "[a] ***particularly important and useful aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes. Such probes*** would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified." (col. 25, lines 11-16) This is evident from the "Summary of the Invention" portion of the Patent which, as discussed above, states: "In accordance with the practices of this invention nucleotides are modified . . . preparatory for the preparation therefrom of ***nucleotide probes suitable for attachment to or incorporation into DNA or other nucleic acid material***." (col. 2, lines 57-62 (emphasis added)) The application as originally filed specifically stated that the "modified polynucleotides" are ***capable of use as "hybridization probes,"*** including "gene mapping in situ hybridization" and

> provides a "General Protocol For Probe Detection Via *In Situ*, Colony, or Northern / Southern Hybridization Methods." ('060 Patent Application as filed, pp. 27-29) ***Based on the above, one skilled in the art would understand that the oligo- and polynucleotide probes of the '060 Patent claims must be capable of use as hybridization probes.***

(emphasis added.) MPI's Brief fails to mention any of this because it knows that a construction consistent with the above would be dispositive of its prior art invalidity defenses.

IV. A Construction That Is Properly Congruent With Enzo's Actual And Complete Statements To The PTO Should Dispose Of MPI's Prior Art Defenses

The reason why Enzo recently presented its claim construction to the PTO in the Response was to overcome MPI's arguments that its prior art references anticipate the Claims. Enzo's arguments do exactly that because none of MPI's references teach that the mononucleotide to be first labeled must also be capable of subsequent incorporation into an oligo- or polynucleotide for use as a ***hybridization probe***. This is detailed in the Response and Rokita Declaration which are attached hereto and incorporated/repeated below in support of Enzo's cross-motion for summary judgment of no anticipation:

The Draper Prior Art Does Not Anticipate: As detailed in the Response/Rokita Declaration, and repeated here for purposes of responding to MPI's Motion and Enzo's cross-motion, the Draper reference that MPI relies upon as allegedly invalidating prior art to Claims 1 and 3 of the '060 patent, does not anticipate the Claims for at least the reason that it does not disclose hybridization probes and would be entirely unsuitable for such purpose because the resulting Draper product (1) destabilizes the ability of the polynucleotide to complex, i.e., hybridize, with complementary sequences; (2) creates polynucleotides with lowered stability; (3) uses chemistry that causes nucleotides within the polynucleotide to change which would interfere with base pairing; (4) leads to random labeling that is not useful for a hybridization probe; (5) uses a synthetic polynucleotide which has no naturally occurring complement it could hybridize

and detect; (6) uses a label that may destabilize pairing with bases in a complementary nucleic acid; and (7) uses a labeling method that is not suitable to label natural mRNA. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.) In fact, the focus of Draper is to study interactions between nucleic acids and ribosomes (i.e., proteins), not to create a probe for hybridization to a complementary nucleic acid sequence. (Ex. 12 at 10; Ex. 13 ¶ 10; Ex. 4 at pp. 1774.) Moreover, Draper "does not first prepare a labeled mononucleotide and then incorporate the labeled mononucleotide into a probe as required by the claims of the '060 Patent" as MPI's incomplete construction would require. (Ex. 12 at 9-10; Ex. 14 at 187-189.) Indeed, under a heading entitled "Synthesis of Labeled Polynucleotides," Draper describes a method for attaching fluorescent labels to a nucleotide residue already within an intact synthetic polynucleotide called Poly(C). (Ex. 12 at 9-10 (citing Ex. 4 at pp. 1775-1776); Ex. 13 ¶¶ 10, 17; Ex. 14 ¶ 187.) Draper thus reacts a polynucleotide, not a mononucleotide, with a label. (*Id*.) Accordingly, under either of Enzo's or MPI's proposed constructions, Draper cannot anticipate.[4] *Union Carbide*, 308 F.3d at 1189.

The Eshaghpour Prior Art Does Not Anticipate: As detailed in the Response/Rokita Declaration, and repeated here for purposes of responding to MPI's Motion and Enzo's cross-motion, MPI's allegedly invalidating Eshaghpour reference does not anticipate Claims 1 and 2 of the '060 patent for at least the reason that it does not disclose hybridization probes, but is instead

[4] Because the Draper and Eshaghpour references teach the same mode of operation that MPI has represented to be employed by ULYSIS products, i.e., to "label only oligo- or polynucleotides," they should fall outside the scope of the claims for the same reason MPI contends its product does. (MPI Brief at 10.) Draper's mention of a labeled monophosphate nucleotide (called NBF-CMP) is likewise non-anticipating because used NBF-CMP to measure concentration, and did not attempt (nor could he) to incorporate that nucleotide into an oligo- or polynucleotide for use as a hybridization probe because it would need to be converted to a different compound before incorporation. (Ex. 4 at 1776; Ex. 14 at ¶ 189.) This separate and dispositive reason that Draper does not anticipate should be considered as part of any claim scope disclaimer determination. *Cordis Corp.*, 511 F.3d at 1177; *Seachange*, 413 F.3d at 1372; *Read*, 970 F.2d at 824.

concerned with the study of protein-DNA interactions. (Ex. 12 at 14(citing Ex. 5, Abstract); Ex. 13 at ¶ 19; Ex. 14 at ¶ 195; Ex. 18 at 142:19-143:6, 146:7-147:18.) Moveover, "Eshaghpour cannot anticipate because it does not first label a mononucleotide and then incorporate that labeled nucleotide into a probe but instead adds the detectable label directly to the intact DNA polymer." (Ex. 12 at 15 (citing Ex. 5 at Fig. 1, p. 1489).; *see also* Ex. 13 at ¶ 20; Ex. 14 ¶ 194.) Indeed, Eshaghpour does not add a labeled mononucleotide to a polynucleotide (*e.g.*, DNA), but rather *first* attaches a thiouridine nucleotide analog to the 3' end of a DNA strand and *then* links labels onto that nucleotide analog. (*Id*.) Thus, again, even under either of Enzo's and/or MPI's proposed constructions, Eshaghpour cannot anticipate (see fn. 4, supra). *Union Carbide*, 308 F.3d at 1189.[5]

The Faust Prior Art Does Not Anticipate: As detailed in the Response/Rokita Declaration, and repeated here for purposes of responding to MPI's Motion and Enzo's cross-motion, the Faust reference relied on by MPI also does not anticipate Claim 1 of the '060 patent because the labeled nucleotide analog which it describes is not capable of incorporation into an oligo- or polynucleotide, and thus would also not be capable of use as a hybridization probe. (Ex. 12 at 16-17; Ex. 13 at ¶¶ 22-24; Ex. 14 ¶¶ 199-200; Ex. 18 at 150:24-151:5.) Indeed, as confirmed by Dr. Rokita, Faust is a study of nucleic acid interactions with proteins, not other

[5] Eshaghpour also does not anticipate for the separate and dispositive reasons presented in the Response and supported by statements of Drs. Rokita, Sinden and Keana (MPI's witness), as well as the '060 patent specification (*see* Ex. 12 at 14-16; Ex. 13 ¶¶ 18-19; Ex. 14 ¶ 194; Ex. 18 at 140:2-142:2; Ex. 2 at col. 20, line 59 to col. 21, line 43, col. 31, line 16; Ex. 5 at pp. 1490) that Eshaghpour describes labeling a pyrimidine analog, i.e., 4-thiouridine, which is not within the scope of the '060 patent Claims calling for a "pyrimidine, purine or 7-deazapurine" to be labeled, nor anywhere mentioned in the '060 patent. Furthermore, the inclusion of 4-thiouridine on a deoxyribose would not be an "otherwise naturally-occurring nucleotide[]" as required by the Court for the '955 patent which is incorporated into the '060 patent (*see Enzo Biochem, Inc. v. Amersham PLC*, 439 F. Supp. 2d 309, 314 (S.D.N.Y 2006). (Ex. 12 at 16.) These arguments must be considered as part of any claim scope disclaimer determination. *Cordis*, 511 F.3d at 1177; *Seachange*, 413 F.3d at 1372; *Read*, 970 F.2d at 824.

nucleic acids, and has a bulky label without a linker that would interfere with the base pairing necessary for incorporation into a nucleic acid. (Ex. 13 ¶¶ 21-24; Ex. 12 at 16-17; Ex. 14 ¶¶ 197-199.) Accordingly, for these reasons alone, Faust does not disclose all of the limitations of the properly construed Claims and, thus, cannot anticipate. *Union Carbide*, 308 F.3d at 1189.[6]

In sum, Enzo respectfully submits that its proposed claim construction, if adopted by the Court, effectively disposes of MPI's prior art invalidity defenses and warrants grant of partial summary judgment on those anticipation defenses.

CONCLUSION

For all of the foregoing reasons, Enzo respectfully submits that the Court should: (i) reject MPI's incomplete claim construction, (ii) adopt Enzo's claim construction, and (iii) grant Enzo's motion for partial summary judgment of validity of the '060 patent.

Dated: August 12, 2013

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[6] By itself, the specific purine *analog* disclosed by Faust is not covered by Claim 1 for the same reasons as discussed for Eshaghpour analog—analogs other than 7-deazapurine are not within the scope of claim 1 and inclusion of a non-natural nucleobase in a ribonucleotide does not comport with this Court's previous claim construction on the '060-incorporated '955 patent—and thus cannot anticipate it. (*See* fn. 5; *see also* Ex. 12 at 17-18; Ex. 13 ¶ 21; Ex. 14 ¶¶ 197-198; Ex. 18 at 148:11-17; Ex. 3 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.) Faust also does not anticipate for the separate and dispositive reasons presented in the Response and elsewhere (*see* Ex. 12 at 16-18; Ex13 ¶ 22; Ex. 14 ¶ 199) including that it is not capable of incorporation into a polynucleic acid and would not result in a probe capable of forming stable complexes with complementary sequences. These arguments by Enzo should be considered as part of any claim scope disclaimer determination. *Cordis* at 1177; *Seachange* at 1372; *Read* at 824.